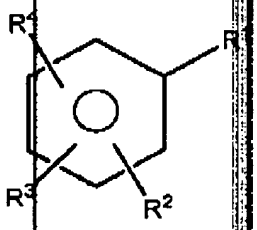
KCC 4749.2
K.C. 16,858.2
PATENT

1. Rejection of Claims 1, 11, and 14-20 Under 35 U.S.C. §103(a)

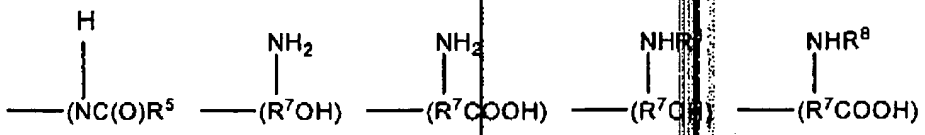
Reconsideration is requested of the rejection of claims 1, 11, and 14-20 under 35 U.S.C. §103(a) as being unpatentable over DE 1204777 in view of D'Augustine, et al. (U.S. 6,416,779).

Claim 1 is directed to an exoprotein inhibitor for inhibiting production of exoproteins from Gram positive bacteria in and around the vagina. The exoprotein inhibitor comprises a non-absorbent substrate for insertion into a vagina being selected from the group consisting of a non-absorbent incontinence device, a barrier birth control device, a tampon applicator, and a douche. The non-absorbent substrate has deposited thereon an effective amount of a first active ingredient having the general formula



wherein R^1 is selected from the group consisting of H, 

$-OR^5$, $-R^6C(O)H$, $-R^6OH$, $-R^6COOH$, $-OR^6OH$, $-OR^6COOH$, $-C(O)NH_2$,



and NH_2 and salts thereof; R^5 is a monovalent saturated or unsaturated aliphatic hydrocarbyl moiety; R^6 is a divalent saturated or unsaturated aliphatic hydrocarbyl moiety; R^7 is a trivalent saturated or unsaturated aliphatic hydrocarbyl moiety; R^8 is a monovalent substituted or unsubstituted saturated or unsaturated aliphatic hydrocarbyl moiety which may or may not be interrupted with hetero atoms; R^2, R^3, and R^4 are independently selected from the group consisting of H, OH, COOH, and $-C(O)R^9$; R^9 is hydrogen or a monovalent saturated or unsaturated aliphatic hydrocarbyl moiety. The first active ingredient is effective in inhibiting the production of exoprotein from Gram positive bacteria.

DE 1204777 ('777) discloses a method of increasing the bactericidal action of hexachlorophene. The method includes combining hexachlorophene with 1% (by weight) to 95% (by weight) benzoic acid, aniline, or benzamide. Specifically, '777 discloses that the addition of benzamide, in a concentration of from 50% (by weight of the mixture with hexachlorophene) to 91% (by weight of the mixture with hexachlorophene), increased the germicidal activity against *Staphylococcus aureus* by 37% to 100% and at the same time, accelerated the killing action. Additionally, benzoic acid and aniline showed a synergistic bactericidal effect when combined with hexachlorophene.

As noted by the Office in the Office action dated November 28, 2005, '777 fails to disclose a non-absorbent substrate for insertion into the vagina being selected from the group consisting of a non-absorbent incontinence device, a barrier birth control device, a tampon applicator, and a douche. In an

attempt to find each and every element of claim 1 as required by the M.P.E.P. for a determination of *prima facie* obviousness, the Office cites the D'Augustine et al. reference for combination with '777.

D' Augustine et al. disclose devices, methods, and compositions for treating vaginal fungal, bacterial, viral, and parasitic infections by intravaginal or transvaginal administration of therapeutic and/or palliative antifungal, antibacterial, antiviral or parasiticidal drugs to the vagina or to the uterus. Specifically, a device such as a tampon, tampon-like device, vaginal ring, pessary, cervical cup, vaginal sponge, intravaginal tablet, or intravaginal suppository, delivers the drug, which can be in the form of a paste, cream, ointment, microcapsule, solution, powder, or gel having a sufficient thickness to maintain prolonged vaginal epithelium and mucosa contact. In one embodiment, the drug can be incorporated into a cream, lotion, foam, paste, ointment, or gel which can be applied to the vagina using an applicator.[1]

In order for the Office to show a *prima facie* case of obviousness, M.P.E.P. §2143 requires that the Office must meet three criteria: (1) the prior art references must teach or suggest all of the claim limitations; (2) there must be some suggestion or motivation, either in the references themselves or in the knowledge generally available to one of ordinary skill in the art, to combine the references, and (3) there must be some reasonable expectation of success. The Office has failed to

[1] D' Augustine et al. at column 18, lines 24-26.

meet its burden under (2) above, as there is no motivation or suggestion to combine the '777 and D'Augustine et al. references to arrive at Applicants' claim 1.

As noted in M.P.E.P. §2142, in establishing obviousness, the Office must show references that reach all of the claimed limitations along with some motivation or suggestion, either in the references themselves or in knowledge generally available to one skilled in the art, to combine the references and arrive at the claimed subject matter.[2] The mere fact that the references can be combined to arrive at the claimed subject matter does not render the resultant combination obvious, unless the prior art also suggests the desirability of the combination. In re Mill, 916 F.2d 680, 16 USPQ2d 1430 (Fed. Cir. 1990). A close reading of the cited references clearly indicates that one skilled in the art would not have been so motivated and, without Applicants' disclosure as a blueprint (which the Office had the benefit of utilizing), such a combination of the '777 and D'Augustine et al. references would not have been made.[3]

---

[2]As further set forth in M.P.E.P. §2143.01, obviousness can only be established by combining or modifying the teachings of the prior art to produce the claimed invention where there is some teaching, suggestion, or motivation to do so found either explicitly or implicitly in the reference itself, or in the knowledge generally available to one of ordinary skill in the art.

[3]M.P.E.P. §2142 further provides that "In order to reach a proper determination under 35 U.S.C. §103(a) the Examiner must step backward in time and into the shoes worn by the hypothetical "person of ordinary skill in the art" when the invention was unknown and just before it was made. In view of Applicants'

The Office asserts that, as the '777 reference teaches benzamide as an effective inhibitor of *Staphylococcus*[4] and

---

disclosure must be put aside in reaching this determination, yet kept in mind in order to determine the "differences." The tendency to resort to "hindsight" based upon Applicants' disclosure is often difficult to avoid due to the very nature of the examination process. However, as stated by the Federal Circuit, impermissible hindsight must be avoided and the legal conclusion must be reached on the basis of the facts gleaned from the prior art. Grain Processing Corp. v. American-Maize-Products, Co., 840 F.2d 902, 904 (Fed. Cir. 1988).

[4] It is noted that the Office states that the '777 reference discloses benzamide as an inhibitor of *Staphylococcus*. Applicants respectfully note that the '777 reference discloses using **hexachlorophene and benzamide together as an antibacterial agent** and not as an inhibitor of *Staphylococcus*. Further, it is worth noting at this time that the first active ingredient used in the exoprotein inhibitor of claim 1 of the present invention is not acting as an antibacterial agent as apparently understood by the Office. As mentioned in Applicants' specification, the first active ingredient acts to **inhibit the production of exoproteins** from Gram positive bacteria, but does not seek to kill the bacteria as the killing of bacteria is non-selective and the "good" bacteria needed to maintain a healthy vagina would also be killed. Thus, the non-selective killing of bacteria could actually be very harmful to the vagina and could cause serious health problems. This is significant. The first active ingredient as claimed in claim 1 of the present invention actually seeks not to act as an antibacterial agent as claimed by the Office, but seeks to only prevent the production of potentially harmful by-products of bacteria, while allowing the bacteria to live. It is also noted that the '777 reference does not suggest or disclose that a composition having the general formula of the first active ingredient of claim 1 can act in such a manner.

In the Office action dated May 17, 2006, the Office states that Applicants' arguments regarding inhibiting the exoprotein production without killing the bacteria are not persuasive as

D'Augustine discloses effective delivery of desired drugs through non-absorbent vaginal devices, it would have been obvious for one skilled in the art at the time of the instant invention to add the benzamide of the '777 reference to the non-absorbent devices of D'Augustine for inhibiting bacterial infections in the vaginal area. With all due respect, Applicants submit that this is not a convincing line of reasoning as to why the combination of these references would have been obvious to one skilled in the art at the time of the invention. Specifically, why would one skilled in the art pick the composition of the '777 reference over all of the other non-toxic, antibacterial compositions in the art, particularly when the D'Augustine et al. provide numerous suitable antibacterial compositions to use with their non-absorbent devices and do not point to any need for alternatives?

D' Augustine et al. simply teach compositions that can be

---

the instant claims do not exclude killing of the bacteria while inhibiting exoprotein production. Further, even though the references cited recognize antibacterial effect, it is to be noted that while the ultimate effect of an antibacterial agent is killing the bacteria, such an effect includes inhibiting proteins. With all due respect, Applicants assert that the Office is combining the first and second prongs of MPEP §2143, that of teaching each and every limitation and providing motivation or suggestion to modify/combine the references. As '777 teaches the use of benzamide as an antibacterial (and not as an inhibitor of exoprotein production as required in claim 1), one skilled in the art, looking to the '777 reference, would not and could not be motivated to combine the benzamide of '777 with the absorbent devices of D'Augustine et al. This motivation prong is separate and distinct from the prong

used as antibacterials to treat bacterial infections of the vagina and devices for delivering the compositions; and even provide several commercially acceptable antibacterial compositions. The D' Augustine et al. reference fails to provide a reason why one skilled in the art would choose another antibacterial over those listed in the D' Augustine et al. reference or disclosed elsewhere in the art. The '777 reference is directed to improving the bactericidal action of hexachlorophene by combining hexachlorophene with other antibacterial compounds, in one embodiment, with benzamide in a pH range of 6.0 to 6.8. No where in the '777 reference is it disclosed that the antibacterial composition including benzamide alone is effective in the treatment of vaginal fungal, bacterial, viral, and parasitic infections in and around the vagina. Specifically, the '777 reference discloses that the amides, such as benzamide, alone ordinarily have little or no germicidal or fungicidal properties. As such, one reading the '777 reference would not and could not be motivated to use benzamide alone for inhibiting *S. aureus*.

Furthermore, while D'Augustine discloses the use of numerous antimicrobials and antifungals, no where in the D'Augustine reference is it disclosed to use hexachlorophene as an antibacterial or antifungal. As such, why would one skilled in art, reading the '777 reference, believe benzamide would provide a synergistic effect when combined with the antibacterials of D'Augustine? It appears the Office is

requiring the cited reference to teach or suggest each and every

suggesting that benzamide would be expected to provide improved germicidal and fungicidal properties to all antimicrobial agents. One skilled in the art simply would not and could not make this assumption with a reasonable expectation of success.

Furthermore, in the Response section of the Office action dated May 17, 2006, the Office states that "Applicants' arguments are not persuasive because '777 suggests a synergistic increase in the antibacterial activity by the addition of compounds such as benzamide, aniline, etc., which is a very small group of compounds as opposed to [Applicants'] argument that '777 suggests numerous other compounds."[5] With all due respect, Applicants note to the Office that, as discussed above, Applicants' argued that there was no motivation to combine the references as the Office has failed to provide a convincing line of reasoning why one skilled in the art would be motivated to choose another antibacterial over the numerous other antibacterials listed in the D'Augustine et al. reference. Specifically, the D'Augustine et al. reference discloses antibacterials such as metronidazole, clindamycin, ampicillin, amoxicillin, tetracycline, and doxycycline, as well as numerous other anti-viral, anti-fungal, and anti-trichomona agents.[6]

Furthermore, the D'Augustine et al. reference is directed to treating infections such as *Haemophilus vaginitus* and *Cornebacterium vaginitis* caused by anaerobic bacteria such as *Gardnerella vaginalis* or *Mycoplasma hominus*. No where in the

---

limitation of the claims.
[5] Office action dated May 17, 2006 at page 3.
[6] *See* the D'Augustine et al. reference at column 10, lines 16-31.

D'Augustine et al. reference are infections caused by *Staphylococcus aureus* taught or suggested. As such, one skilled in the art would not, and could not, be motivated to use the anti-bacterials of '777, which, as shown in every working Example of '777, are effective against *Staphylococcus aureus*, over the anti-bacterials discussed in the D'Augustine et al. reference directed to treating the infections caused by *Gardnerella vaginalis* or *Mycoplasma hominus*.

As such, one skilled in the art would not, and could not, be motivated to use the compounds of '777 over any other antibacterial compounds in the intravaginal devices of D' Augustine et al. to arrive at each and every limitation of Applicants' claim 1.

With all due respect, it appears that the Office has used impermissible hindsight analysis and reconstruction when combining the '777 and D'Augustine, et al. references. There is simply no motivation or suggestion to combine the '777 reference with the D'Augustine reference to arrive at each and every limitation of claim 1.

As there is no motivation or suggestion to combine the '777 and D' Augustine et al. references to arrive at each and every limitation of claim 1, claim 1 is patentable over '777 in view of D'Augustine et al.

Claims 11 and 14-20 depend directly from claim 1. As such, claims 11 and 14-20 are patentable over '777 in view of D'Augustine et al. for the same reasons as claim 1 set forth above, as well as for the additional elements they require.

2. Rejection of Claims 1, 11, 14-20, and 22-32 Under 35 U.S.C. §103(a)

Reconsideration is requested of the rejection of claims 1, 11, 14-20, and 22-32[7] under 35 U.S.C. §103(a) as being unpatentable over Syverson et al. (U.S. 5,612,045) in view of DE 1204777('777).

Claim 1 is discussed above. Additionally, the '777 reference is discussed above.

As discussed above, '777 fails to disclose a non-absorbent substrate for insertion into the vagina being selected from the group consisting of a non-absorbent incontinence device, a barrier birth control device, a tampon applicator, and a douche. Additionally, the '777 reference fails to disclose ethers as a second active ingredient as required in claims 22-32. In an attempt to find each and every element of claim 1 and further each and every element of claims 22-32, the Office attempts to combine 5,612,045 ('045) with the '777 reference. Specifically, the Office states that it would have been obvious for one of ordinary skill in the art to combine the benzamide compound of '777 with the toxin inhibiting ether compounds of '045 and apply the compounds to the feminine hygiene products of '045. Furthermore, the Office states that while '045 does not disclose the specific non-absorbent articles of claim 1, absent any unexpected results with respect to the non-absorbency of the

[7] Applicants respectfully note that in the Office action dated November 28, 2005, claim 32 was found to contain allowable subject matter but was objected to as being dependent upon a rejected base claim.

articles, it would have been within the scope of a skilled artisan to use either non-absorbent or absorbent articles for incorporating the compounds of '777 and '045.

As noted above, a *prima facie* case of obviousness under M.P.E.P. §2143 requires that the Office must meet three criteria: (1) the prior art references must teach or suggest all of the claim limitations; (2) there must be some suggestion or motivation, either in the references themselves or in the knowledge generally available to one of ordinary skill in the art, to combine the references, and (3) there must be some reasonable expectation of success. The Office has failed to meet its burden under (1) and (2) above, as the cited references alone or in combination fail to show an exoprotein inhibitor comprising a non-absorbent substrate and there is no motivation or suggestion to combine and/or modify the '777 and '045 references to arrive at Applicants' claim 1.

As noted above, neither of the cited references expressly teaches a non-absorbent substrate selected from the group consisting of non-absorbent incontinence device, a barrier birth control device, a tampon applicator, and a douche for use in inhibiting exoprotein production in and around the vagina. While Applicants agree with the Office that the '045 reference teaches absorbent articles including compounds to inhibit exoprotein production, Applicants assert that no where in '045 it is suggested or taught that the same compounds could be used in the same manner on a non-absorbent substrate to inhibit exoprotein production.

In the Response section of the Office action dated May 17,

2006, the Office states that the '045 reference teaches that the compounds effective against *S. aureus* can be used on absorbent as well as non-absorbent fibers of the devices, such as covers or wrappers of the vaginal devices including tampons. With all due respect, Applicants disagree with the Office's interpretation of the '045 reference. A close reading of the '045 references supports that the absorbent devices, such as a tampon, may be made of various fiber blends including both absorbent and nonabsorbent fibers. Further these absorbent devices may or may not have a suitable cover or wrapper. No where, however, is it taught or suggested in the '045 reference to use the compounds on the cover or wrapper of the tampon or solely on any non-absorbent substrate. As such, the Office has not shown a convincing line of reasoning for one skilled in the art to use the compounds of the '045 reference on non-absorbent substrates to inhibit exoprotein production.

Furthermore, even if one skilled in the art, reading '045, would be motivated to use the compounds of '045 on a non-absorbent substrate (which Applicants assert they would not be so motivated), there is no motivation or suggestion to combine the cited references and arrive at each and every limitation of claim 1.

As noted above, '045 simply teach ether compositions that can be used with absorbent articles such as catamenial tampons to inhibit the exoproteins of Gram positive bacteria. Specifically, '045 is directed to solving the problem of toxic shock syndrome, which is caused by TSST-1, an exoprotein

produced by *S. aureus* found in the vagina.[8] The inventors of '045 found that their ether compounds could be used to inhibit exoprotein produced by *S. aureus* without harming the natural flora of the vagina.[9] No where in the '045 reference is killing of *S. aureus* bacteria taught or suggested as a desired method of controlling exoprotein production. As such, one skilled in the art would not, and could not, be motivated to use the compounds of the '777 reference, specifically, the combination of hexachlorophene and benzamide, which is shown in the '777 reference to kill *S. aureus*, in the absorbent devices of '045, specifically designed to inhibit exoprotein production by *S. aureus* without killing the bacteria.

Additionally, while the '045 reference generally teaches that the ether compositions may employ additional active materials such as supplementary antimicrobials, anti-parasitic agents, antipruritics, astringents, local anaesthetics, or anti-inflammatory agents[10] for combination therapy, no where in the '045 reference is it taught or suggested to use an antibacterial to kill *S. aureus* bacteria. As such, the '045 reference fails to provide a reason why one skilled in the art would choose benzamide disclosed in '777 as the additional antibacterial over any of the other numerous antibacterials disclosed elsewhere in the art.

Additionally, as noted above, the '777 reference is directed to improving the bactericidal action of hexachlorophene

---

[8] *See* U.S. 5,612,045 at column 2, lines 6-11.
[9] *See* U.S. 5,612,045 at column 3, lines 1-6.
[10] U.S. 5,612,045 at column 5, lines 21-27.

by combining hexachlorophene with other antibacterial compounds, specifically, in one embodiment, with benzamide. No where in the '777 reference is it disclosed to use the antibacterial composition, specifically benzamide, for the inhibition of exoprotein production in and around the vagina. Furthermore, no where is it disclosed in '777 that the antibacterial benzamide would be safe to use internally in humans. As such, one skilled in the art would not, and could not, have been motivated to use the '777 composition on an absorbent substrate such as a catamenial tampon, which would inevitably, and unavoidably, contact the sensitive mucosal membrane of the inner vagina.

In the instant Office action, the Office states that if Applicants' argument is that benzamide would unavoidably and inevitably harm the sensitive mucosal membrane of the inner vagina, then the same argument should hold true for the claimed invention because the instant invention also employs the same benzamide. With all due respect, it appears that the Office has misunderstood Applicants' argument. The Applicants' are not asserting that benzamide is harmful to the sensitive mucosal membrane of the inner vagina. Specifically, Applicants' argue that as no where in the '777 reference is it taught or suggested that benzamide or any of its antibacterial compounds are suitable for use in the vagina, without using the Applicants' disclosure as a blueprint (which, as noted above, such use has been ruled by the Federal Circuit as being improper hindsight reconstruction), there would be no motivation or suggestion to use benzamide in the absorbent devices of '045. As such, there is simply no motivation or suggestion to combine the '045

reference with the '777 reference to arrive at each and every limitation of claim 1.

As no where in the cited references, is an exoprotein inhibitor comprising a non-absorbent substrate as required in claim 1 taught or suggested and further, there is no motivation or suggestion to combine the '045 and '777 references to arrive at each and every limitation of claim 1, claim 1 is patentable over '045 in view of '777.

Claims 11, 14-20, and 22-32 depend directly or indirectly from claim 1. As such, claims 11, 14-20, and 22-32 are patentable over '045 in view of '777 for the same reasons as claim 1 set forth above, as well as for the additional elements they require.

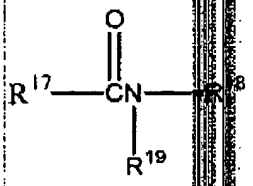
3. Rejection of Claims 1, 11, 14-20, and 48-55 Under 35 U.S.C. §103(a)

Reconsideration is requested of the rejection of claims 1, 11, 14-20, and 48-55 under 35 U.S.C. §103(a) as being unpatentable over Syverson et al. (U.S. 5,685,872) in view of DE 1204777('777).

Claim 1 is discussed above. Additionally, the '777 reference is discussed above.

As discussed above, '777 fails to disclose a non-absorbent substrate for insertion into the vagina being selected from the group consisting of a non-absorbent incontinence device, a barrier birth control device, a tampon applicator, and a douche.

Additionally, the '777 reference fails to disclose active agents having the general formula:



wherein R^{17}, inclusive of the carbonyl carbon, is an alkyl group having 8 to 18 carbon atoms, and R^{18} and R^{19} are independently selected from hydrogen or an alkyl group having from 1 to about 12 carbon atoms which may or may not be substituted with groups selected from ester groups, ether groups, amine groups, hydroxyl groups, carboxyl groups, carboxyl salts, sulfonate groups, sulfonate salts, and mixtures thereof as a second active ingredient as required in claims 48-55. In an attempt to find each and every element of claim 1 and further each and every element of claims 48-55, the Office attempts to combine 5,685,872 ('872) with the '777 reference. Specifically, the Office states that it would have been obvious for one of ordinary skill in the art to combine the benzamide compound of '777 with the toxin inhibiting compounds of '872 and apply the compounds to the feminine hygiene products of '872. Furthermore, the Office states that while '872 does not disclose the specific non-absorbent articles of claim 1, absent any unexpected results with respect to the non-absorbency of the articles, it would have been within the scope of a skilled artisan to use either non-absorbent or absorbent articles for incorporating the compounds of '777 and '872.

Similar to the arguments made above, the Office has again failed to meet its burden under (1) and (2) of M.P.E.P. §2143 for a *prima facie* case of obviousness, as the cited references alone or in combination fail to show an exoprotein inhibitor comprising a non-absorbent substrate and there is no motivation or suggestion to combine and/or modify the '777 and '872 references to arrive at Applicants' claim 1.

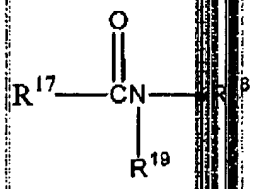
As noted above, neither of the cited references expressly teaches a non-absorbent substrate selected from the group consisting of non-absorbent incontinence device, a barrier birth control device, a tampon applicator, and a douche for use in inhibiting exoprotein production in and around the vagina. While Applicants agree with the Office that the '872 reference teaches absorbent articles including compounds to inhibit exoprotein production, Applicants assert that no where in '872 it is suggested or taught that the same compounds could be used in the same manner on a non-absorbent substrate to inhibit exoprotein production.

As in the rejection over the '777 reference in combination with the '045 reference, the Office responds to Applicants' arguments by initially stating that the '872 reference teaches that the compounds effective against *S. aureus* can be used on absorbent as well as non-absorbent fibers of the devices, such as covers or wrappers of the vaginal devices including tampons. Similar to above, Applicants again disagree with the Office's interpretation of the reference. Similar to the '045 reference, a close reading of the '872 reference supports that the absorbent devices, such as a tampon, may be made of various

fiber blends including both absorbent and nonabsorbent fibers. Further, these absorbent devices may or may not have a suitable cover or wrapper. No where, however, is it taught or suggested in the '872 reference to use the compounds on the cover or wrapper of the tampon or solely on any non-absorbent substrate. As such, the Office has not shown a convincing line of reasoning for one skilled in the art to use the compounds of the '872 reference on non-absorbent substrates to inhibit exoprotein production.

Furthermore, even if one skilled in the art, reading '872, would be motivated to use the compounds of '872 on a non-absorbent substrate (which Applicants assert they would not be so motivated), there is no motivation or suggestion to combine the cited references and arrive at each and every limitation of claim 1.

'872 simply teach nitrogen containing compounds having the general formula:



wherein R^{17}, inclusive of the carbonyl carbon, is an alkyl group having 8 to 18 carbon atoms, and R^{18} and R^{19} are independently selected from hydrogen or an alkyl group having from 1 to about 12 carbon atoms which may or may not be substituted with groups selected from ester groups, ether groups, amine groups, hydroxyl

groups, carboxyl groups, carboxyl salts, sulfonate groups, sulfonate salts, and mixtures thereof that can be used with absorbent articles such as catamenial tampons to inhibit the exoproteins of Gram positive bacteria. Specifically, '872 is directed to solving the problem of toxic shock syndrome, which is caused by TSST-1, an exoprotein produced by *S. aureus* found in the vagina.[11] The inventors of '872 found that their compounds could be used to inhibit exoprotein production by *S. aureus* without altering the natural flora found in the vaginal area.[12] No where in the '872 reference is killing of *S. aureus* bacteria taught or suggested as a desired method of controlling exoprotein production. As such, one skilled in the art would not, and could not, be motivated to use the compounds of the '777 reference in the absorbent devices of '872, specifically designed to inhibit exoprotein production by *S. aureus* without killing the bacteria.

Additionally, while the '872 reference generally teaches that their nitrogen containing compounds may employ additional active materials such as supplementary antimicrobials, anti-parasitic agents, antipruritics, astringents, local anaesthetics, or anti-inflammatory agents[13] for combination therapy, no where in the '872 reference is it taught or suggested to use an antibacterial to kill *S. aureus* bacteria. As such, the '872 reference fails to provide a reason why one skilled in the art would choose benzamide disclosed in '777 as

---

[11] *See* U.S. 5,685,872 at column 2, lines 7-12.
[12] *See* U.S. 5,685,872 at column 3, lines 4-9.
[13] U.S. 5,685,872 at column 5, lines 3[illegible]41.

the additional antibacterial over any of the other numerous antibacterials disclosed elsewhere in the art.

As noted above, the '777 reference is directed to improving the bactericidal action of hexachlorophene by combining hexachlorophene with other antibacterial compounds, specifically, in one embodiment, with benzamide. No where in the '777 reference is it disclosed to use the antibacterial composition, specifically benzamide, for the inhibition of exoprotein production in and around the vagina. Furthermore, no where is it disclosed in '777 that the antibacterial benzamide would be safe to use internally in humans. As such, one skilled in the art would not, and could not, have been motivated to use the '777 composition on an absorbent substrate such as a catamenial tampon, which would inevitably, and unavoidably, contact the sensitive mucosal membrane of the inner vagina.

In the instant Office action, the Office states that if Applicants' argument is that benzamide would unavoidably and inevitably harm the sensitive mucosal membrane of the inner vagina, then the same argument should hold true for the claimed invention because the instant invention also employs the same benzamide. With all due respect, it appears that the Office has misunderstood Applicants' argument. The Applicants' are not asserting that benzamide is harmful to the sensitive mucosal membrane of the inner vagina. Specifically, Applicants' argue that as no where in the '777 reference is it taught or suggested that benzamide or any of its antibacterial compounds are suitable for use in the vagina, without the use of Applicants' disclosure as a blueprint (which, as noted above, the Federal

Circuit has ruled such use as improper hindsight reconstruction), there would be no motivation or suggestion to use benzamide in the absorbent devices of '872. As such, there is simply no motivation or suggestion to combine the '872 reference with the '777 reference to arrive at each and every limitation of claim 1.

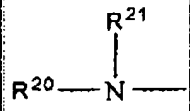
As no where in the cited references, is an exoprotein inhibitor comprising a non-absorbent substrate as required in claim 1 taught or suggested and further, there is no motivation or suggestion to combine the '872 and '777 references to arrive at each and every limitation of claim 1, claim 1 is patentable over '872 in view of '777.

Claims 11, 14-20, and 48-55 depend directly or indirectly from claim 1. As such, claims 11, 14-20, and 48-55 are patentable over '872 in view of '777 for the same reasons as claim 1 set forth above, as well as for the additional elements they require.

4. Rejection of Claims 56-62 Under 35 U.S.C. §103(a)

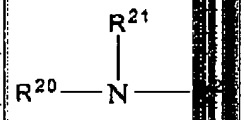
Reconsideration is requested of the rejection of claims 56-62 under 35 U.S.C. §103(a) as being unpatentable over Syverson et al. (U.S. 5,618,554) in view of DE 4204777('777).

Claims 56-62 depend indirectly from claim 1 and further require a second active ingredient having the general formula:



wherein R^{20} is an alkyl group having from about 8 to about 18 carbon atoms and R^{21} and R^{22} are independently selected from the group consisting of hydrogen and alkyl groups having from 1 to about 18 carbon atoms and which can have one or more substitutional moieties selected from the group consisting of hydroxyl, carboxyl, carboxyl salts and imidazoline. Claim 1, which is discussed above, has not been rejected under 103(a) as being unpatentable over 5,618,554 ('554) in view of '777. As such, claims 56-62, which depend from claim 1, are patentable for the same reasons as claim 1, as well as for the additional elements they require.

The '777 reference, which is discussed above, fails to disclose a non-absorbent substrate for insertion into the vagina being selected from the group consisting of a non-absorbent incontinence device, a barrier birth control device, a tampon applicator, and a douche. Additionally, the '777 reference fails to disclose active agents having the general formula:



wherein R^{20} is an alkyl group having from about 8 to about 18 carbon atoms and R^{21} and R^{22} are independently selected from the group consisting of hydrogen and alkyl groups having from 1 to about 18 carbon atoms and which can have one or more

substitutional moieties selected from the group consisting of hydroxyl, carboxyl, carboxyl salts and imidazoline as a second active ingredient as required in claims 56-62. In an attempt to find each and every element of claims 56-62, the Office attempts to combine 5,618,554 ('554) with the '777 reference. Specifically, the Office states that it would have been obvious for one of ordinary skill in the art to combine the benzamide compound of '777 with the toxin inhibiting compounds of '554 and apply the compounds to the feminine hygiene products of '554. Furthermore, the Office states that while '554 does not disclose the specific non-absorbent articles of claim 1, absent any unexpected results with respect to the non-absorbency of the articles, it would have been within the scope of a skilled artisan to use either non-absorbent or absorbent articles for incorporating the compounds of '777 and '554.

The cited references alone or in combination fail to show an exoprotein inhibitor comprising a non-absorbent substrate and there is no motivation or suggestion to combine and/or modify the '777 and '554 references to arrive at Applicants' claims 56-62. As such, the Office has failed to make a *prima facie* case of obviousness under M.P.E.P. §2143.

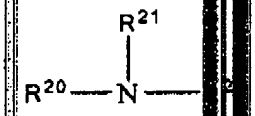
As noted above, neither of the cited references expressly teaches a non-absorbent substrate selected from the group consisting of non-absorbent incontinence device, a barrier birth control device, a tampon applicator, and a douche for use in inhibiting exoprotein production in and around the vagina. While Applicants agree with the Office that the '554 reference teaches absorbent articles including compounds to inhibit

exoprotein production, Applicants assert that no where in '554 it is suggested or taught that the same compounds could be used in the same manner on a non-absorbent substrate to inhibit exoprotein production.

In the Response section of the Office action dated May 17, 2006, the Office states that the '554 reference teaches that the compounds effective against *S. aureus* can be used on absorbent as well as non-absorbent fibers of the devices, such as covers or wrappers of the vaginal devices including tampons. Similar to above, Applicants again disagree with the Office's interpretation of the reference. Similar to the '045 reference, a close reading of the '554 reference supports that the absorbent devices, such as a tampon, may be made of various fiber blends including both absorbent and nonabsorbent fibers. Further, these absorbent devices may or may not have a suitable cover or wrapper. No where, however, is it taught or suggested in the '554 reference to use the compounds on the cover or wrapper of the tampon or solely on any non-absorbent substrate. As such, the Office has not shown a convincing line of reasoning for one skilled in the art to use the compounds of the '554 reference on non-absorbent substrates to inhibit exoprotein production.

Furthermore, even if one skilled in the art, reading '554, would be motivated to use the compounds of '554 on a non-absorbent substrate (which Applicants assert they would not be so motivated), there is no motivation or suggestion to combine the cited references and arrive at each and every limitation of claims 56-62.

'554 simply teaches nitrogen containing compounds having the general formula:



wherein R^{20} is an alkyl group having from about 8 to about 18 carbon atoms and R^{21} and R^{22} are independently selected from the group consisting of hydrogen and alkyl groups having from 1 to about 18 carbon atoms and which can have one or more substitutional moieties selected from the group consisting of hydroxyl, carboxyl, carboxyl salts and imidazoline that can be used with absorbent articles such as feminenial tampons to inhibit the exoproteins of Gram positive bacteria. Specifically, '554 is directed to solving the problem of toxic shock syndrome, which is caused by TSST-1, an exoprotein produced by *S. aureus* found in the vagina.[14] The inventors of '554 found that their compounds could be used to inhibit exoprotein production by *S. aureus* without significantly imbalancing the natural flora present in the vaginal tract.[15] Nowhere in the '554 reference is killing of *S. aureus* bacteria taught or suggested as a desired method of controlling exoprotein production. As such, one skilled in the art would not, and could not, be motivated to use the compounds of the '777 reference in the absorbent devices of '554, specifically

[14] *See* U.S. 5,618,554 at column 2, lines 8-13.

designed to inhibit exoprotein production by *S. aureus* without killing the bacteria.

Additionally, while the '554 reference generally teaches that their nitrogen containing compounds may employ additional active materials such as supplementary antimicrobials, anti-parasitic agents, antipruritics, astringents, local anaesthetics, or anti-inflammatory agents[16] for combination therapy, no where in the '554 reference is it taught or suggested to use an antibacterial to kill *S. aureus* bacteria. As such, the '554 reference fails to provide a reason why one skilled in the art would choose benzamide disclosed in '777 as the additional antibacterial over any of the numerous antibacterials disclosed elsewhere in the art.

As noted above, the '777 reference is directed to improving the bactericidal action of hexachlorophene by combining hexachlorophene with other antibacterial compounds, specifically, in one embodiment, with benzamide. No where in the '777 reference is it disclosed to use the antibacterial composition, specifically benzamide, for the inhibition of exoprotein production in and around the vagina. Furthermore, no where is it disclosed in '777 that the antibacterial benzamide would be safe to use internally in humans. As such, one skilled in the art would not, and could not, have been motivated to use the '777 composition on an absorbent substrate such as a

[15] *See* U.S. 5,618,554 at column 3, lines 41-46.

catamenial tampon, which would inevitably, and unavoidably, contact the sensitive mucosal membrane of the inner vagina.

In the instant Office action, the Office states that if Applicants' argument is that benzamide would unavoidably and inevitably harm the sensitive mucosal membrane of the inner vagina, then the same argument should hold true for the claimed invention because the instant invention also employs the same benzamide. With all due respect, it appears that the Office has misunderstood Applicants' argument. As noted above, the Applicants' are not asserting that benzamide is harmful to the sensitive mucosal membrane of the inner vagina. Specifically, Applicants' argue that as no where in the '777 reference is it taught or suggested that benzamide or any of its antibacterial compounds are suitable for use in the vagina, without the use of Applicants' disclosure as a blueprint (which, as noted above, the Federal Circuit has ruled such use as improper hindsight reconstruction), there would be no motivation or suggestion to use benzamide in the absorbent device of '554. As such, there is simply no motivation or suggestion to combine the '554 reference with the '777 reference to arrive at each and every limitation of claim 1.

As no where has the cited reference taught or suggested an exoprotein inhibitor comprising a non-absorbent substrate as required in claims 56-62 and further, there is no motivation or

[16] U.S. 5,618,554 at column 5, lines 5[illegible]60.

suggestion to combine the '554 and '777 references to arrive at each and every limitation of claims 56-62, claims 56-62 are patentable over '554 in view of '777.

5. Rejection of Claims for Obviousness-type Double Patenting over U.S. Patent 6,821,999

Reconsideration is requested of the rejection of claims 1, 11, 14-20, and 22-68 under the judicially created doctrine of obviousness-type double patenting in view of claims 1-4 of U.S. Patent 6,821,999 in view of any one of U.S. Patent Nos. 5,612,045, 5,685,872, or 5,618,554. In particular, the Office has stated that the claims of the instant application are not patentably distinct from the claims of U.S. Patent 6,821,999 because the patented claims are directed to a method of inhibiting the production of TSST-1 from Gram positive bacteria located in and around the vagina by exposing the vaginal bacteria to a vaginal cleansing formulation comprising thiomalonate and a second active ingredient comprising the general formula (II) that includes the first active compounds of the instant claims.

In response thereto, Applicants have enclosed herewith a Terminal Disclaimer in accordance with 37 C.F.R. 1.130(b) and 37 C.F.R. 1.321(c) to obviate the rejection. Accordingly, Applicants respectfully request the obviousness-type double patenting rejection be withdrawn.

In view of the above, Applicants respectfully request favorable reconsideration and allowance of all pending claims. The Commissioner is hereby authorized to charge any fee

deficiency in connection with this Letter To Patent And Trademark Office to Deposit Account Number 19-1345 in the name of Senniger Powers.

Respectfully submitted,

Christopher M. Goff, Reg. No. 41,785
SENNIGER POWERS
One Metropolitan Square, 16th Floor
St. Louis, Missouri 63102
314-231-5400

CMG/JMB/dhm

Via facsimile (571) 273-8300

This Page is Inserted by IFW Indexing and Scanning Operations and is not part of the Official Record

BEST AVAILABLE IMAGES

Defective images within this document are accurate representations of the original documents submitted by the applicant.

Defects in the images include but are not limited to the items checked:

- ☐ BLACK BORDERS
- ☐ IMAGE CUT OFF AT TOP, BOTTOM OR SIDES
- ☐ FADED TEXT OR DRAWING
- ☐ BLURRED OR ILLEGIBLE TEXT OR DRAWING
- ☐ SKEWED/SLANTED IMAGES
- ☐ COLOR OR BLACK AND WHITE PHOTOGRAPHS
- ☐ GRAY SCALE DOCUMENTS
- ☑ LINES OR MARKS ON ORIGINAL DOCUMENT
- ☐ REFERENCE(S) OR EXHIBIT(S) SUBMITTED ARE POOR QUALITY
- ☐ OTHER: _____

IMAGES ARE BEST AVAILABLE COPY.
As rescanning these documents will not correct the image problems checked, please do not report these problems to the IFW Image Problem Mailbox.